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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/821,227	SCALICE et al.
Examiner	**Art Unit**
James L. Grun, Ph.D.	1641

-- The MAILING DATE of this communication appears n the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-10* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1641.

The drawings are objected to for the following reasons: the panels of Figs. 2, 3, and 7 are not separately labelled. Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Submission of corrected drawings may no longer be held in abeyance pending the indication of allowable subject matter. Failure to take corrective action within the set period will result in **ABANDONMENT** of the application. Direct any inquiries concerning drawing review to the Drawing Review Branch at (703) 305-8404.

The disclosure is objected to because of the following informalities: the brief description of drawings 2, 3, and 7, and all reference to said drawings in the specification must indicate the panel of the Figure which is described or to which the reader is being referred, e.g. the Figures should be described and cited as Figure 2A, or Fig. 2B, or Figs. 2A-2B. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

The specification is objected to and claims 3, 4, 6-8, and 10 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are: (1) known and readily available to the public; (2) reproducible from the written description; or, (3) deposited in compliance with the criteria set forth in 37 CFR §§ 1.801-1.809.

It is unclear if cell lines which produce antibodies having the exact chemical identity and properties of the antibodies designated CRP5-23 (PTA-1354) and C23id2-6.3 (PTA-1353) are known and publicly available, or can be reproducibly isolated without undue experimentation. Accordingly, filing of evidence of the reproducible production of the cell lines and antibodies necessary to practice the instant invention or filing of evidence of deposit is required. Without a publicly available deposit of the above cell lines, one of skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: the claimed cell line; the cell lines which produce the chemically and functionally distinct antibodies claimed; and/or, the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event. For example, very different V_H chains can combine with the same V_L chain to produce antibody binding sites with

nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_L sequences to produce antibodies with very similar properties. These observations indicate that divergent variable region sequences, both in and out of complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. Therefore, it would require undue experimentation to reproduce the claimed monoclonal antibody species chemically as produced by the hybridomas designated CRP5-23 (PTA-1354) and C23id2-6.3 (PTA-1353). A suitable deposit of the hybridomas would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See the criteria set forth in 37 CFR §§ 1.801-1.809.

If the deposits are made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty, that the biological materials will be irrevocably and without restriction or condition released to the public upon the issuance of a patent and that the biological materials will be replaced should they ever become non-viable, would satisfy the deposit requirement made herein.

If the deposits have not been made under the Budapest Treaty, then in order to certify that the deposits meet the criteria set forth in 37 CFR §§ 1.801-1.809, applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposits will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) the deposits were viable at the time of deposit; and,

(e) the deposits will be replaced if they should ever become non-viable.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 3 and 4, "The method" lacks antecedent basis. It is believed that applicant intended the claims to depend on either of claims 1 or 2, rather than upon claims 8 or 9 as recited. These claims have been so treated by the examiner for examination on the merits herein.

In claims 1-5, 9, and 10, the interrelationships of the components are not clear because essential relationships of the components have been omitted, amounting to a gap between the components and, in the method claims, the steps of the method. For example, it is not clear that, as disclosed, the anti-idiotypic antibody binds to the anti-human C-reactive protein antibody and inhibits antigen binding thereto.

In claim 1 and claims dependent thereupon, "the amount" lacks antecedent basis and "an immobilized a low affinity" is not clear.

In claim 2 and claims dependent thereupon, "the amount" lacks antecedent basis.

In claim 4, "is antibody is capable" is not clear.

In claim 5, "where" should be --wherein--.

Claims 3, 4, 6-8, and 10 are vague in the absence of recitation of deposit accession number to clearly identify the antibody/hybridoma because, absent the recitation of deposit accession numbers, it is not clear what structure and properties are encompassed by the named antibodies.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 9 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. There is no indication that the product as claimed is isolated and no claimed degree of purity for the product which would indicate "the hand of man". See, for example, the elicitation of anti-idiotypic antibodies in tumor-bearing mice taught in Goldstein (U.S. Pat. No. 4,699,880). Thus, the product as claimed is considered a product of nature which is non-statutory subject matter.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 6-8 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over either of Kilpatrick et al. (Mol. Immunol. 19: 1159, 1982) or Siegel et al. (WO 91/00872).

Either of Kilpatrick et al. or Siegel et al. teach a number anti-human C-reactive protein monoclonal antibodies and, in particular, teach the HD2-4 anti-human C-reactive protein monoclonal antibody and hybridoma producing same which appear to have properties consistent with those of the monoclonal antibody and hybridoma named CRP5-23. If not, it would have been obvious to have elicited additional antibodies with the properties of the HD2-4 antibody, produced by a hybridoma, guided by the disclosures of the references. Further, the Patent and Trademark Office does not have the facilities and resources to provide the *factual* evidence needed in order to establish that there is a difference, in the first place, between the reagents of the prior art and those instantly disclosed and, that if there is such a difference, that such a difference would have been considered

unexpected, i.e. unobvious, by one of ordinary skill in the art. The burden is upon applicant to present such factual evidence. See e.g. In re Best (195 USPQ 430 (CCPA 1977)) or Ex parte Phillips (28 USPQ2d 1302 (BPAI 1993)).

Claims 1-5, 9, and 10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Englebienne et al. (J. Immunological Meth. 191: 159, 1996) in view of any of Goldstein (U.S. Pat. No. 4,699,880), Maggio (U.S. Pat. No. 4,828,981), or Potocnjak et al. (U.S. Pat. No. 5,219,730), and further in view of Siegel et al. (WO 91/00872).

Englebienne et al. teach a competitive immunoassay for determination of human C-reactive protein. In contrast to the invention as instantly claimed, the reference teaches antigen analog as the competitor and does not teach monoclonal antigen-specific or anti-idiotypic antibodies.

Any of Goldstein, Maggio, or Potocnjak et al. teach the general applicability of competitive immunoassays using monoclonal antibodies specific for a target antigen and monoclonal anti-idiotypic antibodies specific for the antigen-specific monoclonal antibody as the competitor with target antigen in a sample for binding to the antigen-specific monoclonal antibody.

In addition to the teachings of Siegel et al. set forth previously, the reference teaches the use of the monoclonal antibodies in competitive immunoassays (e.g. pages 11-13) and kits therefor.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have substituted monoclonal antibody specific for antigen, such as those taught in Siegel et al. including the HD2-4 monoclonal antibody, and a monoclonal anti-idiotypic antibody

elicited thereto in the competitive immunoassays of Englebienne et al. motivated by the benefits for this notoriously old and well known substitution taught in any of Goldstein, Maggio, or Potocnjak et al. It would have been obvious to formulate the reagents of Englebienne et al., as modified, into a kit since that is conventional for convenience, economy, and reproducibility, for example, as taught in Siegel et al.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (703) 308-3980. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (703) 305-3399.

The phone numbers for official facsimile transmitted communications to TC 1600, Group 1640, are (703) 872-9306, or (703) 305-3014, or (703) 308-4242. Official After Final communications, only, can be facsimile transmitted to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. The above inquiries, or requests to supply missing elements from Office communications, can also be directed to the TC 1600 Customer Service Office at phone numbers (703) 308-0197 or (703) 308-0198.

James L. Grun, Ph.D.
September 30, 2003

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
Group 1641